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Applicants: Mark Ledeboer et al.
Application No.: 10/657,811

REMARKS

The Claim Amendments

Applicants have canceled claims 2-4, 7 and 11-14. Applicants have amended claim 1 to incorporate subject matter from canceled claims 2-4, 7 and 15, wherein support for this amendment may be found. Applicants have amended claims 15-18 to correspond the claims to amended claim 1. Support may be found throughout the specification and in the originally-filed claims. Applicants have amended claims 20-23 to more clearly recite particular methods of treatment and additional therapeutic agents. Support for these amendments may be found throughout the specification and in the originally-filed claims.

These claim amendments are made expressly without waiver of applicants' rights to continue to prosecute and to obtain claims to the canceled subject matter either in this application or in other applications claiming benefit herefrom.

The Response

The Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 1-17 and 19-23 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that the limitation "R^2 is **substituted** or unsubstituted cycloalkyl" does not indicate which chemical groups the cycloalkyl may be substituted with.

Applicants have amended claim 1 to recite specific substitutions for the cyclohexyl or norbornyl cycloalkyl groups, thus obviating this rejection.

The Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 20, 21 and 23 under 35 U.S.C. §112, first paragraph. The Examiner acknowledges that the specification enables methods of treating ischemic and inflammatory disorders of the central nervous system as well as a pharmaceutical composition comprising a compound of claim 1 and an additional pharmaceutical agent for treating ischemia or inflammation, but states that the

specification does not reasonably provide enablement for treating neurodegenerative, neurological or immunological disorders or for pharmaceutical compositions directed to treating such disorders.

Applicants have amended claim 20 to recite a composition comprising an additional therapeutic agent for treatment of stroke, which the Examiner acknowledges is enabled by the specification. Applicants have amended claim 21 to recite a method of treating disorders that are acknowledged by the Examiner to be enabled by the specification. Applicants have also amended claim 23 to recite further administering an additional therapeutic agent for treatment of stroke, which is also clearly enabled by the specification.

The Rejection Under 35 U.S.C. §103(a)

The Examiner has rejected claims 1-2 and 4-23 under 35 U.S.C. 103(a) as allegedly being unpatentable over Green et al. WO 01/12621 (hereafter "the '621 application") in view of Silverman, *The Organic Chemistry of Drug Design and Drug Action*, 1992, Academic Press, pp. 19-23 (hereafter "Silverman"). The Examiner states that formula IA in the '621 application in which the groups R^2 and G are CH_2(heterocyclyl) and aryl, respectively and Q is 2-aminopyrimidine. Further, the Examiner states that specific embodiments in the '621 application include those in which G is phenyl or 4-fluorophenyl, Q is 2-aminopyrimidine, R^2 is cyclohexyl or 4-cyclohexanol and R^1 is CH_2(piperidinyl). The Examiner also states that the '621 application also provides methods for using the compounds and pharmaceutical compositions. The Examiner acknowledges that the '621 application does not explicitly disclose the specific compounds, pharmaceutical compositions or methods of the instant claims. However, the Examiner states that Silverman discloses that the substitution of bioisosteres in an existing molecules produces derivatives having similar biological properties. The Examiner states it would have been obvious to one of ordinary skill in the art at the time of the invention to produce the compounds of formula I, and pharmaceutical compositions comprising the compounds, because the compounds fall within the limitations of the structures disclosed by the '621

application and the specific functional groups defined in the claims are all disclosed in various embodiments of the '621 application, particularly compounds XIA-39 to XIA-53. Applicants traverse.

As acknowledged by the Examiner, the '621 application does not teach or suggest specific compounds that fall within the claimed genus. In addition, neither the '621 application nor Silverman teach or suggest the specific claimed combination of substituents on the isoxazole ring. Thus, one skilled in the art would not have been motivated to make the compounds of the instant invention based on the two cited references. Further, the specification teaches that "compounds of the invention unexpectedly and surprisingly exhibit increased potency in the protection of neuronal cells against ischemic injury and as inhibitors in *in vitro* CNS inflammation assays" (see paragraph [0044] on page 11 of the specification). The specification also discloses that certain compounds of the invention exhibited about 35% to about 70% protection in rat model of ischemia (see paragraph [00143] on page 32), greater than 50% protection in an *in vitro* assay of ischemia (see paragraph [00167] on page 35) and IC_{50}s of less than 1 μM in an *in vitro* assay of CNS inflammation (see paragraph [00174] on page 36). Neither the '621 application nor Silverman, either alone or in combination, teaches or suggests compounds having these improved properties for treating CNS disorders. Thus, the unexpectedly better properties possessed by the instantly claimed compounds makes them a non-obvious patentable invention over the '621 application or Silverman.

Double Patenting

The Examiner has rejected claims 1-2, 4-19 and 21-22 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,693,108 (hereafter "the '108 patent") in view of Silverman. Applicants traverse.

The '108 patent is the U.S. equivalent of the '621 application. For the reasons provided above in the response to the 35 U.S.C. §103(a) rejection, applicants submit that the instant claims are non-obvious over the claims of the '108 patent.

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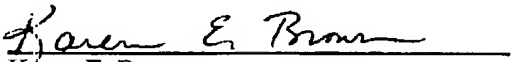
Conclusion

Applicants request that the Examiner enter the above amendments, consider the accompanying arguments, and allow the claims to pass to issue. Should the Examiner deem expedient a telephone discussion to further the prosecution of the above application, applicants request that the Examiner contact the undersigned at his convenience.

Respectfully submitted,



Karen E. Brown
Reg. No. 43,866
Attorney for Applicants
c/o Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, Massachusetts 02139
Tel: (617) 444-6168
Fax: (617) 444-6483